Henkel LOCTITE

201-15121B

ROBUST SUMMARY

PHYSICAL/CHEMICAL ELEMENTS

1) MELTING POINT -30°C

REFERENCES
Coover, H.W., Dreifus, D.W., and O'Connor, J.T., in Handbook of Adhesives, Irving Skeist editor, Van Nostrand Reinhold, 1990.

2) BOILING POINT

TEST SUBSTANCE:	Loctite Super Bonder 420. (Ethyl cyanoacrylate >99%)
Remarks	This is typical of monomeric ethyl cyanoacrylate as produced.
METHOD	OPPTS 830.7950
GLP (Y/N)	Not applicable
Year(study performed)	2003
RESULTS	210 °C (410 °F) at 760mm Hg
Remarks	Boiling point reported is the temperature at which the vapor pressure equals 760 torr (one atmosphere) in the vapor pressure determination reported below.

REFERENCES
Unpublished study, Phoenix Chemical Laboratory Inc., August 22, 2003.

3) VAPOR PRESSURE

TEST SUBSTANCE:	Loctite Super Bonder 420. (Ethyl cyanoacrylate >99%)
Remarks	This is typical of monomeric ethyl cyanoacrylate as produced.
METHOD	OPPTS 830.7950
GLP (Y/N)	Yes
Year(study	2003
RESULTS	0.31torr @ 20 °C (68 ° F)

REFERENCES
Unpublished study, Phoenix Chemical Laboratory Inc., August 22, 2003.

4) PARTITION COEFFICIENT

TEST SUBSTANCE:	Loctite Super Bonder 420. (Ethyl cyanoacrylate >99%)
Remarks	This is typical of monomeric ethyl cyanoacrylate as produced.
METHOD	OPPTS 830.7550
GLP (Y/N)	Yes
Year(study performed)	2002
Temperature	25°C
RESULTS	Log Pow Not determined. No ethyl cyanoacrylate could be detected in the water phase.
Remarks	Determination of the partition coefficient was attempted using EPA OPPTS method 830.7550. When the ethyl cyanaocrylate standard solution in n-octanol was being prepared, a white precipitate was observed. This was anticipated because of the long recognized sensitivity of cyanoacrylate esters towards trace quantities of nucleophiles including water, which promote rapid polymerization of the cyanoacrylate esters. The various n-octanol/cyanoacrylate mixtures were intimately contacted with water as required by the protocol for OPPTS 830.7550. Following centrifugation, the concentration of cyanoacrylate in each liquid phase was measured by reverse phase HPLC according to OSHA Method 55. No cyanoacrylate ester could be detected in any of the separated aqueous samples (Detection limit established as 2 µg/ml).
CONCLUSIONS	The partition coefficient for ethyl cyanaocrylate cannot be determined due to its ready polymerization in the presence of moisture.
DATA QUALITY	
Reliabilities	1
REFERENCES	Unpublished study, Datachem Laboratories, 2002.

5) WATER SOLUBILITY

TEST SUBSTANCE:	Loctite Super Bonder 420 (Ethyl cyanoacrylate >99%)
Remarks	This is typical of monomeric ethyl cyanoacrylate as manufactured.
METHOD	OSHA Method 55
GLP (Y/N)	Yes
Year (Study performed)	2002
RESULTS	The study (OPPTS 830.7550) previously described to determine the octanol /water partition coefficient established that due to its tendency to polymerize rapidly on contact with moisture, the actual water solubility of ethyl cyanoacrylate is negligible (< 2µg/ml).
DATA QUALITY	
Reliabilities	1
REFERENCES	Unpublished study, Datachem Laboratories, 2002.

ENVIRONMENTAL FATE AND PATHWAY ELEMENTS

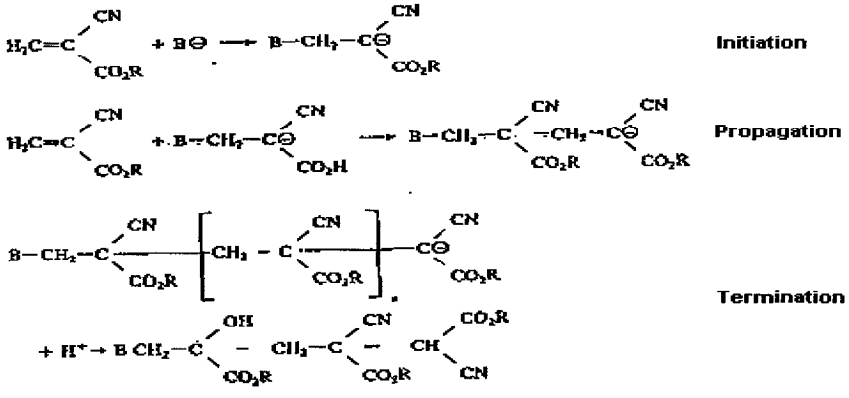
6) PHOTODEGRADATION

Theoretical modeling of the photodegradation of methyl 2-cyanoacrylate is reported in the National Toxicology Program's peer reviewed Hazardous Substance Database (HSDB). Based on the similarity in structure, its conclusions are applicable to ethyl 2-cyanoacrylate. It was estimated that vapor phase methyl 2-cyanoacrylate will be degraded in the atmosphere by reaction with photochemically produced hydroxyl radicals; the half-life for this reaction in air was estimated to be 5 days. It is unclear if this model takes into account the reactive nature of the molecule.

Cyanoacrylate esters are very reactive monomers that rapidly polymerize upon exposure to moisture. In the atmosphere and in biological systems, the available hydroxyl ions initiate rapid polymerization of ethyl cyanoacrylate monomer. The necessity to include polymerization inhibitors in the production distillation system further illustrates the reactive nature of the molecule.

The mechanism of polymerization is provided in Figure 1.

Figure 1



Mechanism of Ionic Polymerization of Cyanoacrylate Esters

The propagation rate constant for ethyl cyanoacrylate has been determined to be between $3x10^5$ and $6x10^5$ L∃mol^{-1}∃s^{-1} at 20°C in tetrahydofuran[1].

The probability of significant atmospheric releases is further reduced by its manufacture in a closed system and its use and distribution patterns. The largest size in which ethyl cyanoacrylate formulations are distributed in commerce in any significant amount is in one pound (454 g) bottles.

These circumstances make significant atmospheric levels of ethyl cyanoacrylate monomer improbable, and the development of any further data of no practical value. To support this data and as suggested by the EPA, AOPWIN modeling has been performed.

[1] D.C. Pepper, B. Ryan, Makromol. Chem 395 1983. In Macromol. Rapid Commun. **17**, 217-227, 1996

AOPWIN MODELING

Type	:	Air
Light source	:	Sun light
Light spectrum	:	Nm
Relative intensity	:	Based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	= .000000000045401 cm^3/(molecule*sec)
Degradation	:	= 50% after 28.271 hour(s)
Deg. product	:	
Method	:	Other (calculated)
Year	:	2003
GLP	:	Not applicable
Test substance	:	Theoretical 100% ethyl cyanoacrylate (7085-85-0) was used for modeling.
Remark	:	Inputs to the program are the CAS No. 7085-85-0, a measured melting point of –30 degrees C, a measured boiling point of 210 degrees C, and a vapor pressure of 0.31 mm Hg. Rerunning the program, inputting only the CAS No. and no measured physical property inputs made no change in the model results for photodegradation. Atmospheric photodegradation is not expected to be a major route of elimination, since the substance has limited volatility.
Reliability	:	(2) Valid with restrictions Data were obtained by EPIWIN modeling.
Flag	:	Critical study for SIDS endpoint
Reference	:	PCA Services, Photodegradation Modeling for Ethyl cyanoacrylate, EPIWIN (3.10) AOP Program (1.90), October 2003.

7) STABILITY IN WATER

Ethyl cyanoacrylate monomer reacts rapidly with moisture to form polymeric ethyl cyanoacrylate. This precluded any attempts to measure its stability in water.

8) TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

Because of the reactive nature of ethyl cyanoacrylate monomer and the manner in which it is distributed in commerce, fugacity information is of no practical value.

First, ethyl cyanoacrylate as a specialty chemical is not stored or transported in large containers, hence, significant release into the water supply is unlikely. Storage in the production facility is in 55 gallon drums (ethyl cyanaocrylate as produced), or 15 gallon plastic or metal containers (as formulated adhesives comprising approximately 90% ethyl cyanoacrylate). The most prevalent package size sold into the industrial market is a one-ounce bottle, followed by 20-gram bottle and then a one pound bottle. Small numbers of 2 kilogram bottles are distributed. Product for the consumer market is marketed in 2, 3, and 5 gram packages. Distribution in these small volume units greatly reduces the possibility of significant spills during transportation. Consistent with the package sizes, manufacturing operations utilizing ethyl cyanoacrylate adhesive apply it "by the drop" or as a small bead, thus, the opportunities for a large spill are limited.

Secondly, as previously demonstrated, ethyl cyanoacrylate monomer reacts upon contact with moisture. A stabilizer must be added to the receiving vessel during production to prevent immediate polymerization. Even after being stabilized for commercial purposes, if exposed to the atmosphere the monomer rapidly polymerizes to form an inert solid polymer. It is on this characteristic that the use of ethyl cyanoacrylate as a finger print developer is based. Polymerization occurs independent of the environmental compartment.

Finally, during the period in excess of 30 years that Loctite has been a leading manufacturer and marketer of ethyl cyanoacrylate and ethyl cyanoacrylate based products there has been, to our knowledge, no significant spill into the environment.

Based on the properties and marketing pattern discussed above and its long safe history in commerce, we maintain that development of information on fugacity is of theoretical value only, and is not justified.

9) BIODEGRADATION

Due to the previously described rapid polymerization, ethyl cyanoacrylate monomer does not exist in the environment in sufficient quantities for biodegradation to take place or for persistence to be an issue.

ECOTOXICITY ELEMENTS

10) ACUTE TOXICITY TO FISH
11) TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)
12) ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)

There is no practical opportunity for aquatic organisms to be exposed to significant volumes of ethyl cyanoacrylate.

First, ethyl cyanoacrylate as a specialty chemical is not stored or transported in large containers making significant release into the water supply unlikely. Storage in the production facility is in 55 gallon drums (ethyl cyanaocrylate as produced), or 15 gallon plastic or metal containers (as formulated adhesives comprising approximately 90% ethyl cyanoacrylate). The most prevalent package size sold into the industrial market is a one-ounce bottle, followed by a 20-gram bottle and then a one pound bottle. Small numbers of 2 kilogram bottles are distributed. Product for the consumer market is sold in 2, 3, and 5 gram packages. Distribution in these small volume units greatly reduces the possibility of significant spills during transportation. Consistent with the package sizes, manufacturing operations utilizing ethyl cyanoacrylate adhesive apply it "by the drop" or as a small bead, thus, the opportunities for a large spill are limited.

Secondly, as previously demonstrated, ethyl cyanoacrylate monomer reacts upon contact with moisture. A stabilizer must be incorporated in the receiving vessel during production to prevent immediate polymerization. Even after being stabilized for commercial purposes, if exposed to the atmosphere it rapidly polymerizes to form an inert solid polymer. It is on this characteristic that the use of ethyl cyanoacrylate as a finger print developer is based. Polymerization occurs independent of the environmental compartment

Based on the combination of these circumstances and that in the period in excess of 30 years that Loctite has been manufacturing ethyl cyanoacrylate products there has been, to our knowledge, no significant spill into the aquatic environment, we maintain that development of aquatic toxicity data is not warranted.

HEALTH ELEMENTS

13) ACUTE TOXICITY

A. Oral

TEST SUBSTANCE	Depend, IS 04E, Product 495, (Ethyl cyanoacrylate >95%, polymethyl methacrylate <5%).
Remarks	Test material was a commercial adhesive formulation representative of the formulations marketed at that time.
METHOD	
Type	Oral LD50 Limit test.
GLP (Y/N)	No (GLP introduced in 1978)
Year (study performed)	1973
Species/Strain	Albino Rats
Sex	Male
No.of animals per sex per dose	6
Vehicle	None
Route of administration	Oral intubation
Test Conditions.	The initial body weight ranged from 206-246 grams. The animals were fasted 18 hours prior to dosing. A single dose of 5000mg/kg was administered. Animals were observed during the day of dosing and daily thereafter for 14 days.
RESULTS	
Value	Oral LD50 >5000mg/kg
Number of deaths	1/6
Time of death	Day 4
Signs of intoxication	Death
Gross autopsy findings	Hemorrhagic lungs. Solid mass in stomach not adhered to stomach wall but too large to pass through pyloric valve. Cardiac portion of stomach distended. Food in intestine as in normal rat. One rat had dilated intestinal blood vessels.
DATA QUALITY	
Reliabilities	2
Remarks	Study not conducted under GLP but essentially the same as OECD 401

REFERENCES

Acute Oral Toxicity in Rats with Depend, IS 04E, (Product 495), Affiliated Medical Research, Inc. Princeton New Jersey, November 15, 1973.

B. Dermal Toxicity

TEST SUBSTANCE	04E, Depend, Product 495, (Ethyl cyanoacrylate >95%, polymethyl methacrylate <5%).
Remarks	Test material was a commercial adhesive formulation representative of the formulations marketed at that time.
METHOD	
Type	Dermal LD50 Limit test.
GLP (Y/N)	No (GLP introduced in 1978)
Year (study performed)	1973
Species/Strain	Albino Rabbits New Zealand Strain
Sex	Male
No.of animals per sex per dose	4
Vehicle	None
Route of administration	Dermal
Test Conditions.	The initial body weight ranged from 2034-2481grams. The animals were clipped free of dorsal hair. A single dose of 2000mg/kg was applied under rubber dental damming held in place with adhesive tape for 24 hours. Animals were observed during the day of dosing and daily thereafter for 14 days. At which time the y were sacrificed and examined for gross pathology.
RESULTS	
Value	Dermal LD50 >2000mg/kg
Number of deaths	0/4
Signs of Intoxication	None
Gross autopsy findings	Bandages and wrapping were initially bonded to skin, however after 14 days bandages were easily peeled off exposing a large open sore at site of application.
DATA QUALITY	
Reliabilities	2
Remarks	Study not conducted under GLP but essentially the same as OECD 402

REFERENCES

Acute Dermal LD50 Test in Rabbits with Depend, IS 04E, (Product 495), Affiliated Medical Research, Inc. Princeton New Jersey, December 5, 1973.

C. Dermal Irritation

TEST SUBSTANCE	Depend, Product 495, (Ethyl cyanoacrylate >95%, polymethyl methacrylate <5%).
Remarks	Test material was a commercial adhesive formulation representative of the formulations marketed at that time.
METHOD	
Type	Primary Dermal Irritation.
GLP (Y/N)	No (GLP introduced in 1978)
Year (study performed)	1973
Species/Strain	Albino Rabbits New Zealand Strain
Sex	Male
No.of animals	6
Vehicle	None
Test Conditions.	Skin on the dorsal surface was shaved free of hair by means of electric clippers. Twelve dorsal test areas were utilized; six were abraded down to, but not through, the dermis, using a hypodermic needle. The remaining test areas were left intact. 1"x1" gauze pads were saturated with 0.5g test liquid and applied to the dermal test areas. The gauze pads were left in place for 24 hours. The test areas were scored for dermal irritation immediately following the 24-hour exposure period and at 72 hours-post exposure, according to the method Draize[1].
RESULTS	The primary Irritation Index was determined to be 0.87. The test material is considered a mild irritant.
DATA QUALITY	
Reliabilities	2
Remarks	Study not conducted under GLP but essentially the same as OECD 404

REFERENCES

Primary dermal Irritation of Depend Adhesive in Rabbits (Product 495), Affiliated Medical Research, Inc., Princeton New Jersey, November 7, 1973.

[1] Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics, Assoc. of Food and Drug Officials of the U.S., Austin Texas, 1959.

D. Eye Irritation

TEST SUBSTANCE	Depend, Product 495, (Ethyl cyanoacrylate >95%, polymethyl methacrylate <5%).
Remarks	Test material was a commercial adhesive formulation representative of the formulations marketed at that time.
METHOD	
Type	Primary Eye Irritation.
GLP (Y/N)	No (GLP introduced in 1978)
Year (study performed)	1973
Species/Strain	Albino Rabbits, New Zealand Strain
Sex	Male
No.of animals	6
Vehicle	None
Test Conditions.	Approximately 0.1ml of the test liquid was introduced into the conjunctival sac of the right eye of each rabbit, the left eye served as an untreated control. The treated eyes were scored against the untreated eye according to the method of Draize[1] at 24, 48, and 72 hours after instillation of test liquid.
RESULTS	The group mean irritation score at 24 hours was 29.33, at 48 hours was 15.33 and at 72 hours was 9.66. According to the Draize evaluation, the test material was considered an irritant to the eye.
DATA QUALITY	
Reliabilities	2
Remarks	Study not conducted under GLP but essentially the same as OECD 405

REFERENCES

Primary Eye Irritation of Depend Adhesive (Product 495), Affiliated Medical Research, Inc. Princeton New Jersey, November 6, 1973.

[1] Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics, Assoc. of Food and Drug Officials of the U.S., Austin Texas, 1959.

E. Acute Inhalation

TEST SUBSTANCE	Superbonder 420, (Ethyl cyanoacrylate >99%)
Remarks	Test material is typical of monomeric ethyl cyanoacrylate as manufactured.
METHOD	
Type	Acute Inhalation
GLP (Y/N)	No (GLP introduced in 1978)
Year (study performed)	1982
Species/Strain	Wistar derived Albino Rats
Sex/No.of animals	5 male, 5 female
Test Conditions	Animals weighing 200-300g were exposed to 1.9g of test material during a 1-hour exposure period. During the first 30 minutes the test material was nebulized into the inhalation chamber after being warmed in a vessel submerged in water at 35-37°C. The temperature of the water bath was decreased to 25°C for the remaining 30 minutes. The concentration was estimated to be 21.11 mg/L/hour determined gravimetrically. Animals were observed for 14 days after exposure.
RESULTS	
Value	Inhalation LC50 <21.11mg/L (4123 ppm)/hour, nominal.
Number of deaths	7/10
Time of death	Days 1,2,2,4,4,3,2
Signs of intoxication	Animals were extremely irritable and showed signs of severe respiratory stress, eye irritation, and skin irritation. Several animals suffered nasal and ocular bleeding during the exposure period.
Autopsy findings	7 animals showed pulmonary, spleenic and intestinal hemorrhage. The remaining animal showed pulmonary and intestinal hemorrhage.
Remarks	The dosing level was determined gravimetrically, and it is unclear the extent to which polymerization was taken into account.
DATA QUALITY	
Reliabilities	2
Remarks	Study not conducted under GLP but essentially the same as OECD 403

REFERENCES

Acute inhalation study Superbonder 420, Ethyl Cyanoacrylate. Product Safety Labs, New Brunswick, NJ. December 14, 1982.

14) GENETIC TOXICITY IN VIVO (CHROMOSOMAL ABERRATIONS)

GENETIC TOXICITY ELEMENTS

14) GENETIC TOXICITY IN VIVO (CHROMOSOMAL ABERRATIONS)
TEST SUBSTANCE

A. MICE

Identity	Ethyl Cyanoacrylate (CAS No. 7085-85-0)
Remarks	Aliquot A57325 (As identified by NTP)

METHOD

Method/guideline followed	Not specified
Type (test type)	Micronucleus induction
GLP (Y/N)	Not Specified
Year (study performed)	1994
Species	Mice
Strain	B6C3F1
Sex	Male
Route of administration	Intraperiotineal
Doses/concentration levels	25, 40, 80, 120, 160mg/kg
Exposure period	72 hours
Statistical methods	Average, and standard error of the mean
- Age at study initiation	Not specified
- No.of animals per dose	5
- Vehicle	Not specified (expected to approximate100% ethyl cyanoacrylate)

Remarks

- Duration of test	72 hours
- Frequency of treatment	3 doses
- Sampling times and number of samples	24hours,
- Control groups and treatment	Control and 5 treatment groups
- Clinical observations performed	None specified
- Organs examined at necropsy	None specified
- Criteria for evaluating	Bone marrow cells, 2000 examined at each dose level
- Criteria for selection of M.T.D.	Two range finding experiments

RESULTS

Effect on mitotic index or PCE/NCE ratio by dose level by sex	None
Genotoxic effects	Negative
NOAEL(NOEL) (C)/LOAEL(LOEL) (C)	Not applicable
Statistical results, as appropriate	Not applicable

Remarks

- Mortality at each dose level by sex	Up to 160mg/kg-none; 3 of 4 dead at 200mg/kg
- Mutant/aberration/mPCE/polyploidy	

frequency, as appropriate	None
- Description, severity, time of onset and duration of clinical signs at each dose level and sex	Not specified
- Body weight changes by dose & sex	Not specified
- Food/water consumption changes by dose and sex	Not specified

CONCLUSIONS

This study was not published by NTP but it was reported in the Federal Register vol 60, page 42987, 1995, that "ethyl cyanoacrylate was not mutagenic in rodent bone marrow micronucleus tests."

DATA QUALITY

Reliabilities	4 (not assignable)
Remarks field for Data Reliability	Insufficient information in results released by NTP
REFERENCES (Free Text)	NTP unpublished results

Remarks This summary was completed at the request of OPPTS in comments[1] on our original HPV submission. It is based on data tables provided by NTP. NTP requested that these data not be included in any formal report, but allowed the conclusions to be referenced as "NTP unpublished results".

[1] EPA Comments on Chemical RTK HPV Challenge Submission: Ethyl Cyanaocrylate, May 28, 2003.

B. RATS

Identity Ethyl Cyanoacrylate (CAS No. 7085-85-0)

Remarks Aliquot A57325 (As identified by NTP)

METHOD

Method/guideline followed	Not specified
Type (test type)	Micronucleus induction
GLP (Y/N)	Not Specified
Year (study performed)	1994
Species	Rats
Strain	Fischer 344
Sex	Male
Route of administration	Intraperiotineal
Doses/concentration levels	25, 625, 1250, 2500mg/kg
Exposure period	72 hours
Statistical methods	Average and standard error of the mean

Remarks

- Age at study initiation	Not specified
- No. of animals per dose	5
- Vehicle	Not specified (expected to be approximately 100% ethyl cyanoacrylate)
- Duration of test	72 hours
- Frequency of treatment	3 doses
- Sampling times and	24 hours
number of samples	Not specified
- Control groups and treatment	Control and 4 treatment groups
- Clinical observations performed	None specified
- Organs examined at necropsy	None specified
- Criteria for evaluating	Bone marrow cells, 2000 examined at each dose level
- Criteria for selection of M.T.D.	Not specified

RESULTS

Effect on mitotic index or PCE/NCE ratio by dose level by sex	None
Genotoxic effects	Negative
NOAEL(NOEL) (C)/LOAEL(LOEL) (C)	Not applicable
Statistical results, as appropriate	Not applicable

Remarks

- Mortality at each dose level by sex	Not specified
- Mutant/aberration/mPCE/polyploidy frequency, as appropriate	None
- Description, severity, time of onset and duration of clinical signs at each dose level and sex	Not specified
- Body weight changes by dose & sex	Not specified
- Food/water consumption changes by dose and sex	Not specified

CONCLUSIONS

This study was not published by NTP but it was reported in the Federal Register Vol 60, page 42987, 1995, that "ethyl cyanoacrylate was not mutagenic in rodent bone marrow micronucleus tests."

DATA QUALITY

Reliabilities	4 (not assignable)
Remarks field for Data Reliability	Insufficient information in results released by NTP
REFERENCES (Free Text)	NTP unpublished results

Remarks: This summary was completed at the request of OPPTS in comments[1] on our original HPV submission. It is based on data tables provided by NTP. NTP requested that these data not be included in any formal report, but allowed the conclusions to be referenced as "NTP unpublished results".

[1] EPA Comments on Chemical RTK HPV Challenge Submission: Ethyl Cyanaocrylate, May 28, 2003.

C. RATS

Identity Ethyl Cyanoacrylate (CAS No. 7085-85-0)

Remarks Aliquot A57325 (As identified by NTP)

METHOD

Method/guideline followed	Not specified
Type (test type)	In vivo Micronucleus induction
GLP (Y/N)	Not Specified
Year (study performed)	1993
Species	Rats
Strain	Fischer 344
Sex	Male
Route of administration	Intraperitoneal
Doses/concentration levels	312.5, 625, 1250, 2500mg/kg
Exposure period	96 hours
Statistical methods	Average and standard error of the mean

Remarks

- Age at study initiation	Not specified
- No. of animals per dose	4
- Vehicle	Not specified (expected to be approximately 100% ethyl cyanoacrylate)
- Duration of test	96 hours
- Frequency of treatment	3 doses
- Sampling times and number of samples	48 hours Not specified
- Control groups and treatment	Control and 4 treatment groups
- Clinical observations performed	None specified
- Organs examined at necropsy	None specified
- Criteria for evaluating	Bone marrow cells, 2000 examined at each dose level
- Criteria for selection of M.T.D.	Not specified

RESULTS

Effect on mitotic index or PCE/NCE ratio by dose level by sex	None
Genotoxic effects	Negative
NOAEL(NOEL) (C)/LOAEL(LOEL) (C)	Not applicable
Statistical results, as appropriate	Not applicable

Remarks

- Mortality at each dose level by sex	Not specified
- Mutant/aberration/mPCE/polyploidy fre quency, as appropriate	None
- Description, severity, time of onset and duration of clinical signs at each dose level and sex	Not specified
- Body weight changes by dose & sex	Not specified
- Food/water consumption changes by dose and sex	Not specified

CONCLUSIONS

This study was not published by NTP but it was reported in the Federal Register Vol 60, page 42987, 1995, that "ethyl cyanoacrylate was not mutagenic in rodent bone marrow micronucleus tests."

DATA QUALITY

Reliabilities	4 (not assignable)
Remarks field for Data Reliability	Insufficient information in results released by NTP
REFERENCES (Free Text)	NTP unpublished results

Remarks This summary was completed at the request of OPPTS in comments[1] on our original HPV submission. It is based on data tables provided by NTP. NTP requested that these data not be included in any formal report, but allowed the conclusions to be referenced as "NTP unpublished results".

[1] EPA Comments on Chemical RTK HPV Challenge Submission: Ethyl Cyanaocrylate, May 28, 2003.

15) GENETIC TOXICITY IN VITRO (GENE MUTATIONS)
TEST SUBSTANCE

Identity	Ethyl Cyanoacrylate (CAS No. 7085-85-0)
Remarks	Aliquot A03722 (As identified by NTP)

METHOD

Method/guideline followed	Haworth et al, Environ Mutagen. 5(suppl. 1): 3-142, 1983.
Type	Gene mutation study,
System of testing	Bacterial
GLP (Y/N)	Not Specified
Year study performed	1993
Species/Strain or cell type and or cell line, bacterial or non-bacterial	Salmonella TA 100, TA1535, TA97
Metabolic activation	Yes
- Species and cell type	Hamster Liver, Rat Liver
- Quantity	5%, 10%, 30% (hamster) & 10%30 (rat)
- Induced or not induced	Induced
Concentrations tested	0, 33, 100, 333, 666, 1000, 1666, 3333, 6666, and 10,000 µg/plate
Statistical Methods	Mean and Standard error reported
- Test Design	
· Number of replicates	3 per test
· Frequency of Dosing	1
· Positive and negative control groups and treatment	Not specified
· Number of metaphases analyzed	Not specified
- Solvent	DMSO
- Description of follow up repeat study	Not specified
Criteria for evaluating results	All negatives are repeated, all positives are repeated for conditionn that elicited positive response

RESULTS

Result	
Cytotoxic concentration	
- With metabolic activation	Not reported
- Without metabolic activation	Not reported
Genotoxic effects	Negative

CONCLUSIONS

This study was not published by NTP but it was reported in the Federal Register Vol 60, page 42987, 1995, that "ethyl cyanoacrylate was not mutagenic in the Ames test."

DATA QUALITY

Reliabilities	4 (not assignable)
Remarks field for Data Reliability	Insufficient information in results released by NTP
REFERENCES	NTP unpublished results

Remarks — This summary was completed at the request of OPPTS in comments[1] on our original HPV submission. It is based on data tables provided by NTP. NTP requested that these data not be included in any formal report, but allowed the conclusions to be referenced as "NTP unpublished results".

[1] EPA Comments on Chemical RTK HPV Challenge Submission: Ethyl Cyanaocrylate, May 28, 2003.

16) REPEATED DOSE TOXICITY
17) TOXICITY TO REPRODUCTION
18) DEVELOPMENTAL TOXICITY/TERATOGENICITY

Alkyl cyanoacrylates are among the most reactive monomers known in anionic polymerization. The mechanism of polymerization is described in the discussion on photodegradation. In the atmosphere and in biological systems, available hydroxyl ions initiate rapid polymerization of ethyl cyanoacrylate monomer. This is evidenced by the rapid bonding by instant adhesives comprising predominantly cyanoacrylate esters to skin or any other surface. This property renders ethyl cyanoacrylate a useful adhesive and makes significant exposure to ethyl cyanoacrylate monomer improbable.

As would be anticipated from this chemistry, dosing animals for repeated dose studies is problematic. Ethyl cyanoacrylate was listed by the Interagency Test Committee as a TSCA 4(e) priority chemical. After preliminary work, NTP [1] recommended its removal from the priority list citing "high reactivity of the chemical and the resulting difficulties in implementing the delivery of an effective concentration of the un-polymerized chemical to the test animals". NTP[2] also reported that they were unable to generate a stable aerosol.

The United Kingdom Health and Safety Executive has published a Risk Assessment Document on methyl and ethyl cyanoacrylate[3]. This risk assessment concluded that there are no grounds for concern for carcinogenicity at exposures below the threshold for chronic inflammatory responses in tissues at the site of contact. In addressing reproductive toxicity, they concluded "due to the reactive nature of ethyl cyanaocrylate, little systemic distribution is predicted following exposure by any physiological route. Furthermore, the overall pattern of toxicity data available suggests that the toxicological effects of ethyl cyanoacrylate would be largely restricted to local site of contact effects on the eyes and respiratory tract."

To address concerns that cyanoacrylates including ethyl cyanoacrylate may act as respiratory sensitizers capable of inducing allergic asthma, Loctite Corporation sponsored two studies. The first was a survey to determine the airborne concentrations of cyanoacrylate in a manufacturing plant[4] and the second was an epidemiological[5] study that investigated the pulmonary effects of repeated occupational exposure to cyanoacrylates. The airborne concentrations determined in the first study provided the basis for the epidemiological study. The epidemiological study provided no evidence that those occupationally exposed to cyanoacrylate vapors during the manufacture and packaging of methyl and ethyl cyanoacrylate adhesives had any chronic pulmonary damage or that ethyl cyanoacrylate acted as a respiratory sensitizer. Subjects who had been exposed for a period of up to 18 years had no increased incidence of pulmonary obstruction compared to an unexposed population. These human exposure data render animal data of little value.

[1] 60 FR 42982-7, 1995
[2] NTP 1998 Annual report Table 6.
[3] Methyl cyanoacrylate and ethyl cyanoacrylate, Risk assessment document, UK Health and Safety Executive HMSO, Norwich UK, 2000.
[4] Paustenbach, D.,et al, Am. Ind. Hyg. Assoc J., **62**, 70-79, 2001.

[5] Goodman M, et al, J. Toxic. & Environ. Hlth Part A , **59**, 135-163, 2000.